

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
26 August 2004 (26.08.2004)

PCT

(10) International Publication Number
WO 2004/071479 A1

- (51) International Patent Classification⁷: **A61K 7/44, 7/42, 7/40, A61P 17/16**
- (21) International Application Number: **PCT/AU2004/000170**
- (22) International Filing Date: 12 February 2004 (12.02.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/447,445 12 February 2003 (12.02.2003) US
- (71) Applicant (for all designated States except US): CONNETICS AUSTRALIA PTY LTD [AU/AU]; 8 Macro Court, Rowville, VIC 3178 (AU).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): HUGGINS, Joan, Kathleen [AU/AU]; Unit 2, 44 Wilson Road, Glen Waverley, VIC 3150 (AU). HOULDEN, Robert, James [AU/AU]; 7 Coilesbourne Court, Kilsyth, VIC 3137 (AU).
- (74) Agent: WATERMARK PATENT & TRADEMARK ATTORNEYS; 290 Burwood Road, Hawthorn, VIC 3122 (AU).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/071479 A1

(54) Title: FILM FOAMING HYDROALCOHOLIC FOAM

(57) Abstract: The present invention provides a foam composition comprising an active agent. In particular, the foam composition produces a water resistant, preferably very water resistant, film upon application

Best Available Copy

FILM FOAMING HYDROALCOHOLIC FOAM

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority to U.S. Provisional Patent Application No. 60/447,445, filed February 12, 2003, the disclosure of which is
5 hereby incorporated by reference in its entirety for all purposes.

BACKGROUND OF THE INVENTION

Topical delivery of active compounds is well known. Unfortunately, many topical delivery formulations are not waterproof or water resistant. Thus, when these active agents are applied to the skin and exposed to moisture, most of the
10 active agents are often washed away from the skin thereby reducing their effectiveness.

There are many challenges in the topical application of active agents. For example, application of active agents should be easy and smooth. Moreover, in some instances the composition should remain within the applied area for a
15 prolonged period even when exposed to moisture to provide a relatively constant amount of the active agent within the applied area.

Water resistant or very water resistant formulations of topical delivery systems are especially desirable because they eliminate the need for reapplication after exposure of the applied area to water, such as after swimming,
20 bathing or excessive perspiration. This is particularly true for sunscreen products.

Sunscreen products provide protection for the human skin against damages of ultraviolet light. Products with various sun protection factor (SPF) values are available, thus allowing consumers to choose the amount of protection desired. While a variety of sunscreen products are available, "water resistant" or
25 "very water resistant" sunscreens are especially desirable because they eliminate the need for reapplication after swimming, bathing or excessive perspiration. Generally "water resistant" sunscreen formulations can undergo at least about 40 minutes of water immersion without significant SPF loss, whereas "very water resistant" sunscreen formulations can undergo at least about 80 minutes of water
30 immersion without significant SPF loss.

Ideally, sunscreen products should be stable and easy to apply, and provide acceptable consistency and skin-feel. The foregoing factors, which are

important to achieving consistent distribution on the skin, even sun protection, along with consumer acceptance and commercial viability, are largely functions of the vehicle which carries the sunscreen agents.

For the above reasons, it is clearly desirable to formulate a topical vehicle
5 that is capable of providing acceptable consistency, skin feel and stability, and is easy to use and apply sunscreen agents, and, thereby, achieve both water resistant character and high-SPF values. The present invention fulfils such needs.

SUMMARY OF THE INVENTION

10 The present invention provides a hydroalcoholic foam that comprises an active agent. Advantageously, the hydroalcoholic foam of the present invention is useful for topical application as it is easy to apply. As such, in one aspect, the present invention provides a composition in a pressurized container for forming a hydroalcoholic foam, wherein the composition comprises:

15 at least one active agent;
a water insoluble film-forming polymer;
a hydroalcoholic foaming agent; and
an aerosol propellant.

In one particular embodiment, the active agent is a sunscreen component.
20 Preferably, the sunscreen component comprises at least one UVB sunscreen and/or at least one UVA sunscreen.

When applied to the skin, the water insoluble polymer forms a thin film of a water resistant, preferably very water resistant, barrier. In this manner, the active agent remains within the applied skin area even when wet.

25 In another aspect, the present invention provides a hydroalcoholic foaming agent which comprises a C₁-C₆ alcohol, water, wax and a surfactant. Preferably, the amount of water present in the composition is greater than the amount of C₁-C₆ alcohol.

These and other objects, embodiments and advantages will become more
30 apparent with reference to the detailed description which follows.

DETAILED DESCRIPTION OF THE INVENTION**I. Definitions**

Unless the context requires otherwise, the terms "active agent", "active compound" and "active component" are used interchangeably herein and refer to
5 a substance having a cosmetic, pharmaceutical, pharmacological or therapeutic effect.

Unless indicated otherwise, a "water resistant" composition includes a "very water resistant" composition.

Unless otherwise indicated, all percentages recited herein are weight
10 percentages, based upon total composition weight excluding the propellant.

Unless otherwise indicated "comprises"/"comprising" and grammatical variations thereof when used in this specification are to be taken to specify the presence of stated features, integers, steps or components or groups thereof, but do not preclude the presence or addition of one or more other features, integers,
15 steps, components or groups thereof.

All disclosures referred to herein are hereby incorporated by reference.

II. General

The present invention provides various topical delivery foam compositions for active agents. In particular, compositions of the present invention are directed
20 to water resistant, preferably very water resistant, topical delivery foam compositions comprising active agents. A water resistant property of the active agent is achieved by applying the foam composition to a desired topical area, e.g., skin, which then forms a thin film of a water resistant layer. The compositions of the present invention are contained in a pressurized container.
25 When the composition is dispensed from the container, it forms a foam structure. The rubbing or shearing action of foam application breaks down the foam structure leaving behind a water resistant film of active agent.

In particular, the composition that is contained within the pressurized container comprises: at least one active agent; a water insoluble film-forming
30 polymer; a hydroalcoholic foaming agent; and an aerosol propellant. The amount of each of these components can vary depending on a wide variety of factors, such as the desired foam characteristics, the degree of water resistance, and the like.

Typically, the pressurized container is any container that has a sufficient mechanical strength to withstand the pressure. The container is generally fitted with a valve, e.g., an upright or inverted valve, and a conventional foam spout actuator.

5 In addition, the present invention provides various aspects related to such compositions, including methods for protecting the skin of a subject from ultraviolet light and the use of the compositions in protecting skin against the negative effects of ultraviolet light.

In certain preferred embodiments, the compositions of the present
10 invention are emulsions. In these instances, oil is preferably the dispersed liquid (the discontinuous phase) and the hydroalcoholic solution is the continuous phase. Typically oil in hydroalcoholic emulsions are difficult to stabilize. Therefore, one advantage of this invention is a stable hydroalcoholic film such as a hydroethanolic foam, and more preferably a stable hydroalcoholic film forming
15 foam.

III. Active Agents

The active agent can be any cosmetic agent or pharmaceutically active agent, including sunscreen components, antibiotics, antifungal agents, antiviral compounds, nicotine, as well as other pharmaceutical or therapeutically active
20 agents that are capable of being used topically. Exemplary antifungal agents that are suitable in compositions of the present invention include, but are not limited to, diols, allylamines (including naftifine and terbinafine), polyene macrolide antibiotics (including amphotericin and nystatin), triazole derivatives (such as fluconazole), fatty acids (such as caprylic and propionic acid), amorolfine,
25 ciclopirox, lamine, benzoic acid, flucytosine, haloprogin, tolnaftate, undecenoic acid and its salts, griseofulvin and imidazole compounds (such as ketoconazole and chlorphenesin (3-(4-Chlorphenoxy) propane-1,2-diol)).

The terms "antibiotic" and "antimicrobial" are used herein interchangeably to refer to a compound that inhibits the growth of, inhibits the virulence of, or kills
30 bacterial cells. Antibiotics include, e.g., substances produced by various species of microorganisms (e.g., bacteria, fungi, and actinomycetes), variants thereof, and synthetic antibacterial agents. A complete list of antibiotics is too long to be included herein, and those of skill in the art are aware of the multitude of

antibiotics that can be used in the present invention. See, e.g., Chambers and Sande, *Antimicrobial Agents: General Considerations in Goodman & Gilman's The Pharmacological Basis of Therapeutics*, Hardman and Limbard eds., (1996); and Kucers, et al., *The Use of Antibiotics: A Clinical Review of Antibacterial, 5 Antifungal, and Antiviral Drugs* Oxford Univ. Press (1997). Suitable antibiotic agents include, but are not limited to, clindamycin, erythromycin, tetracycline, minocycline, doxycycline, penicillin, ampicillin, carbenicillin, methicillin, cephalosporins, vancomycin, and bacitracin, streptomycin, gentamycin, chloramphenicol, fusidic acid, ciprofloxacin and other quinolones, sulfonamides, 10 trimethoprim, dapsone, isoniazid, teicoplanin, avoparcin, synergicid, virginiamycin, cefotaxime, ceftriaxone, piperacillin, ticarcillin, cefepime, cefpirome, rifampicin, pyrazinamide, ciprofloxacin, levofloxacin, enrofloxacin, amikacin, netilmycin, imipenem, meropenem, inezolid, pharmaceutically acceptable salts thereof, and prodrugs thereof. Preferably, the antibiotic agent is clindamycin, erythromycin, 15 tetracycline, minocycline, doxycycline, pharmaceutically acceptable salts thereof, or prodrugs thereof.

In certain preferred aspects, the active agent is a light sensitive drug such as an antibiotic (e.g., amikacin, augmentin amoxicillin, ampicillin, cefazolin, cefoxitin, ceftazidime, ceftiofur, cephalexin, enrofloxacin, florfenicol, gentamicin, 20 imipenem, kanamycin, sarafloxacin, tetracycline, ticarcillin, and tilimicosin) an antifungal or other light sensitive pharmaceutical actives such as tretinoin, isotretinoin, sodium sulfacetamide, calcipotriene and hydroquinone. Those of skill in the art will know of other light sensitive active agents suitable for use in the present invention.

25 Other suitable pharmaceutical agents are well known to one skilled in the art. See, for example, The Merck Index, 13th Ed., 2001, Merck & Co., Inc., Whitehouse Station, NJ, pp. THER-1 to THER-31, which is incorporated herein by reference in its entirety. The compositions of the present invention can comprise a mixture of two or more cosmetic agents and/or pharmaceutically active agents. 30 In this manner, a wide combination of active agents can be used simultaneously. For example, the active agent can be a mixture of a sunscreen component and a light sensitive pharmaceutical agent, e.g., an antibiotic compound. The sunscreen component protects the light sensitive pharmaceutical agent from sun

light. Moreover, the water resistant property allows the subject to pursue active outdoor activities, e.g., swimming and other physical activities, which can cause perspiration, without having the active agent being washed away.

In one particular embodiment of the present invention, the active agent is a 5 sunscreen component. The term "sunscreen component" as used herein includes commonly used ultraviolet ray-blocking compounds. Preferably, the sunscreen component comprises at least one UVB sunscreen and/or at least one UVA sunscreen. More preferably, the sunscreen component comprises at least one UVB sunscreen and at least one UVA sunscreen. As expected, the 10 combination of UVB and UVA sunscreens provide a broad spectrum UV protection. A more detailed discussion of sunscreen agents useful in this invention is provided by Roelandts et al., "A Survey of Ultraviolet Absorbers in Commercially Available Sun Products", Int. J. Dermatol., Vol. 22, pp. 247-255 (May, 1983).

15 In another embodiment, the sunscreen component is preferably selected from the group of: Aminobenzoic acid (4-Aminobenzoic acid); Avobenzone (4-tert-butyl-4-methoxydibenzoylmethane); Benzophenone-2 (Bis(2,4-Dihydroxyphenyl) Methanone); Benzophenone-3 (Oxybenzone); Benzophenone-4 (Sulisobenzone); Benzophenone-5 (Sulisobenzone sodium); Benzophenone-8 (Dioxybenzone);
20 Benzylidene Camphor (3-(4-Methylbenzylidene)-d-1camphor); Cinoxate; Ecamsule (Terephthalylidene dicamphor sulfonic acid); Ethoxylated ethyl 4-aminobenzoic acid (PEG25 PABA); Homosalate (Homomethyl salicylate); Isoamylmethoxycinnamate (Isopentenyl-4-methoxycinnamate); Isopropylbenzyl salicylate; Menthyl anthranilate (Methyl 2-aminobenzoate); Mexoryl XL (phenol,2-
25 (2H-benzotriazol-2-yl)-4-methyl-6[2-methyl-3-[1,3,3,3-tetramethyl-1-[(trimethylsilyl)oxy]disiloxanyl]propyl) Octyl dimethyl PABA; Octinoxate (Octyl methoxycinnamate); Octyl salicylate (2-Ethylhexyl Salicylate); Octocrylene (2-cyano-3,3-diphenyl acrylic acid,2-ethyl hexyl ester); Octyl triazole (2,4,6-Trianalino-(p-Carbo-2'-ethylhexyl-1'oxy)1,3,5-Triazine); Padimate O (2-Ethylhexyl
30 4-dimethylaminobenzoate); Phenylbenzimidazole sulfonic acid (2-Phenylbenzimidazole-5-sulfonic acid) and its potassium, sodium and triethanolamine salts; N,N,N-Trimethyl-4-(oxoborn-3-ylidenemethyl) anilinium methylsulfate; Salicylic acid salts (potassium,sodium and triethanolamine);

Tinosorb M. (2,2'-Methylene-bis-6-(2H-benzotriazol-2yl)-4-(tetramethyl-butyl)-1,1,3,3-phenol); Titanium dioxide; Triethanolamine salicylate; Zinc oxide; and mixtures thereof.

The nature and the amount of sunscreen component present in the 5 composition generally affects the sun protection factor (SPF) of the composition. Thus, a wide SPF range is possible in compositions of the present invention. Typically, however, the amount of a particular sunscreen used is determined by the desired SPF. As such, SPF as low as two (2) and as high as 45 or greater can be achieved by adjusting the amount of sunscreen present in the 10 composition. Generally, however, sunscreens having SPF of about 15 or about 30 are most commonly used. However, it should be appreciated that the sunscreen compositions of the present invention are not limited to any particular SPF values.

The sunscreen component can also be used as an agent to protect light 15 sensitive drugs. Therefore, in one embodiment, the present invention provides a combination of a light sensitive active agent and a sunscreen active agent.

As stated above, the amount of sunscreen component present in compositions of the present invention vary depending on the particular sunscreen component(s) chosen and the SPF desired. Typically, however, compositions of 20 the present invention comprise from about 1 to about 30% by weight of the total composition in the container, including the propellant. Preferably, the amount of sunscreen component present in compositions of the present invention is from about 5 to about 40%. Alternatively, at least about 5%, preferably at least about 10%, of the sunscreen component is present in compositions of the present 25 invention. The amount of sunscreen referred to herein refers to the total amount of all sunscreen components that are present in compositions of the present invention. As such, for a composition comprising a mixture of sunscreen components, the amount of each sunscreen component can vary significantly depending on the desired physical and chemical properties as well as the SPF 30 desired.

IV. Water Insoluble Film-Forming Polymer

Typically, the water insoluble film-forming polymer is preferably a carboxylated acrylic copolymer. Water insoluble carboxylated acrylic copolymers

- including those sold by National Starch and Chemical Corporation under the trade names "Dermacryl", "Amphomer" and "Versacryl" (acrylates/octylacrylamide copolymer) (CFTA), are known to be useful in this invention. Particularly preferred carboxylated acrylic copolymer is a solid copolymer sold under the trade name "Dermacryl-79," which provides satisfactory water resistant and/or very water resistant properties. In addition, "Amphomer," or "octylacrylamide/acrylate/butylaminoethyl methacrylate copolymer," a polymer formed from octylacrylamide, t-butylaminoethyl methacrylate and two or more monomers of acrylic acid, methacrylic acid or any of their simple esters, can also be employed.
- 10 Dermacryl 79 CAS Number 129702-02-9 is a hydrophobic, high molecular weight carboxylated acrylic copolymer.

Advantageously, the carboxylic acid functional groups of the film-forming polymers are at least partially neutralized in order to obtain good dispersion of the film-forming polymer in the aqueous medium. In certain aspects, a percentage of 15 the carboxylic acid groups present in the water insoluble carboxylated acrylic copolymer are neutralized. Preferably, the percentage that is neutralized is between 0% to about 40%. Preferably, the percentage that is neutralized is between about 3% to about 35%, more preferably about 7% to about 33%, and most preferably about 10% to about 30%, such as 10%, 11%, 12%, 13%, 14%, 20 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25%, 26%, 27%, 28%, 29% and 30%.

The carboxylic acid functional groups can be neutralized using a basic compound, such as an inorganic base, such as sodium hydroxide, sodium benzoate or potassium hydroxide, or an amino-alcohol selected for example from 25 2-amino-2-methyl-1-propanol (AMP), triethanolamine, triisopropanolamine (TIPA), monoethanolamine, diethanolamine, tris[2-hydroxy-1-propyl]amine, 2-amino-2-methyl-1,3-propanediol (AMPD), alkaline salts of ethylene diamine tetra acetic acid such as tetrasodium ethylene diamine tetra acetic acid (Na₄EDTA), or 2-amino-2-hydroxymethyl-1,3-propanediol. Lysine, arginine or cystine can also be 30 used as neutralizing agents, or combinations of the foregoing. Preferably, the carboxylated acrylic copolymer is neutralized using sodium benzoate and/or tetrasodium EDTA.

Generally, compositions of the present invention have about 0.01 to about 15 weight percent of a carboxylated acrylic copolymer. The range is preferably from about 0.1% to about 10%, with about 0.5% to about 5% being especially preferred.

5 It is known that these polymers become water dispersible/soluble via neutralization of their carboxyl (i.e., carboxylic acid) groups with a base, e.g., an alkaline material. Thus, in some embodiments of the present invention, a portion of the carboxyl groups in the carboxylated acrylic copolymer is neutralized with a base. In this manner, the amount of organic solvent, e.g., C₁-C₆ alcohol, used in
10 the composition can be reduced significantly.

V. Hydroalcoholic Foaming Agent

The hydroalcoholic foaming agent comprises a C₁-C₆ alcohol, water, wax and a surfactant.

A. Alcohols

15 Suitable C₁-C₆ alcohols include methanol, ethanol, propanol, butanol, pentanol, hexanol and their isomers. However, since methanol is poisonous, for safety reasons ethanol n-propanol or isopropanol are preferred. With ethanol being particularly preferred, such as "SD Alcohol 40" or "SDA 40".

In one particular embodiment, the amount of water in the hydroalcoholic
20 foaming agent is higher than the amount of alcoholic solvent, e.g., C₁-C₆ alcohol. Preferably, the amount of C₁-C₆ alcohol present in the composition is less than about 50% by weight of the total composition, more preferably less than about 40% and most preferably, less than about 30%. Alternatively, the amount of C₁-C₆ alcohol present in the composition of the present invention ranges from about
25 5% to about 40% by weight, preferably from about 10% to about 30% and more preferably from about 15% to about 25%, such as 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, and fractions thereof.

B. Water

Typically at least about 40% of the composition is comprised of water,
30 preferably at least about 45% and more preferably at least about 50%. Alternatively, the amount of water present in the compositions of the present invention generally ranges from about 35 to about 65%, preferably from about 40 to about 60% and more preferably from about 50 to about 55%. Thus, unlike

other conventional water resistant compositions, compositions of the present invention have a significantly higher amount of water than the amount of C₁-C₆ alcohol.

C. Wax

5 Various waxes are suitable for use in the present invention. These include for example, non-ionic self-emulsifying waxes. For example, Polawax GP200 (cetearyl alcohol and PEG-20 stearate) (Croda Surfactants) is a non-ionic self-emulsifying wax that is used in oil-in-water emulsions. The waxy material was used to impart structural support to the foam and to improve the film-forming
10 properties and water resistance of the emulsion on the skin. Other waxes suitable for use in the present invention include, but are not limited to, natural waxes such as animal waxes such as carnauba and bees wax, vegetable waxes, mineral waxes such as petroleum waxes, and synthetic waxes.

D. Surfactants

15 Compositions of the present invention can also include a surfactant system. The presence of surfactant allows emulsification of one or more components that may be otherwise insoluble within the composition. The surfactant system of the invention can comprise a polyoxyalkylene ester of a straight or branched chain fatty acid, polysorbate or mixtures thereof. Preferred
20 polyoxyalkylenes include polypropylene glycol and polyethylene glycol, with the latter being especially preferred.

Useful polyoxyalkylene esters of fatty acid include, but are not limited to, the fatty acid esters of polyoxyethylene glycol sold as a "Cithrol" (Croda) and "Myrij 52" (Uniqema). Useful polysorbate includes Polysorbate 85 sold as "Crillet 25 45" (Croda). The surfactant system can also include combinations of one or more surfactants disclosed herein.

Generally, the total amount of surfactant(s) present in compositions of the present invention ranges from about 0.1 to about 20% by weight. The preferred range is from about 0.5% to about 15%, with about 2% to about 10% being highly
30 preferred.

VI. Optional Components

The compositions of the invention can also include suitable amounts of cosmetically and pharmaceutically acceptable additives, i.e., excipients and/or

chemically active adjuvants, including chelating agents, such as EDTA and its salts, and corrosion protecting agents, such as sodium benzoate, or preservatives.

In addition, other additives such as colorants, thickeners, perfumes, fillers, 5 diluents, carriers, plasticizers, stabilizers, gelling agents, preservatives, supplemental emollients/solvents and the like can also be added.

VII. Use

When dispensed from the container, the compositions of the present invention form a foam structure. When the foam is applied to a desired area, it 10 dries relatively quickly to leave a water resistant or very water resistant active agent film on the skin.

The melting point of the hydroalcoholic foam that is produced from compositions of the present invention is about 35°C or higher. Preferably, the foam melting temperature is about 40°C or higher. An especially preferred foam 15 melting temperature is about 45°C or higher. The term "foam melting temperature" refers to the temperature at which the foam structure breaks down without any application of force, e.g., rubbing.

Additional objects, advantages, and novel features of this invention will become apparent to those skilled in the art upon examination of the following 20 examples thereof, which are not intended to be limiting.

VIII. Examples

1. Example 1

This example illustrates various preferred components to formulate a stable sunscreen foam for use on the scalp, face and body.

25 a) **Sunscreen Component**

Parsol MCX (octinoxate) is a highly effective, oil soluble UV-B absorber with maximum absorption at 308 nm. In addition, Parsol MCX is an excellent solvent for Uvinul M40. A concentration of 7.5%w/w was chosen based on the monograph requirements.

30 Uvinul M40 (oxybenzone) is an oil soluble UV-A and UV-B absorber offering maximum absorption in the short-wave UV-B and UV-A spectra. Uvinul M40 is usually employed as a coabsorber in combination with a specific UV-B

absorber (such as Parsol MCX). Uvinul M40 requires sufficient solubility in emulsions to ensure that re-crystallization does not occur.

Parsol 1789 (butyl methoxydibenzolymethane) is a highly effective oil-soluble UV-A filter. It is often used in conjunction with UV-B filters to provide full-spectrum UV protection. The maximum absorption of Parsol 1789 is at or near 360 nm.

b) Excipients

Polawax GP200 (cetearyl alcohol and PEG-20 stearate) (Croda Surfactants) is a non-ionic self-emulsifying wax that is used in oil-in-water emulsions. The waxy material was used to impart structural support to the foam and to improve the film-forming properties and water resistance of the emulsion on the skin.

Dermacryl® 79 (acrylates/octylacrylamide copolymer) (National Starch & Chemical) is a hydrophobic, high molecular weight, polymer. It was used at a level of about 1.5-2.5%w/w in the formulation. It forms a water resistant or water proof film when applied. Its highly water resistant property was used to produce a water resistant sunscreen product.

Myrij 52 (PEG-40 Stearate) (Uniqema) is a non-ionic emulsifier that was used in conjunction with Crillet 45 to obtain a desired HLB (hydrophobic lipophilic balance) system for the formulation. Myrij 52 is preferred to other emulsifiers because it is a solid waxy material. A concentration of 1.5-2.5% was used based on a HLB screening (using different ratios of Myrij 52 and Crillet 45), and as a result of foam quality optimization.

Crillet 45 (Polysorbate 85) (Croda Surfactants) is an oil-in-water emulsifier. It was used at a concentration of 0.5-1.2% in association with Myrij 52 to achieve a desired HLB.

Sodium Benzoate is a commonly used corrosion inhibitor and about 0.10-0.30% was added to the system to prevent can corrosion during storage.

Disodium EDTA (BASF) is a chelating agent that was added to the system at 0.05-0.20%. It is known to one skilled in the art that Parsol 1789 reacts with metals, particularly Fe^{+2} , during manufacture or storage and develops a red complex that discolors the formulation.

The sunscreen foam formulation is a non-greasy, water resistant, SPF 15 foam product that can be used on the head, face and body. One particular sunscreen component formulation is shown below.

- Parsol MCX – 7.5% w/w (in the absence of propellant)
- 5 Uvinul M40 – 4.0% w/w (in the absence of propellant)
- Parsol 1789 – 2.0% w/w (in the absence of propellant)

The foam melting temperature of the formulation was found to be about 40°C.

c) Water Resistance

Dermacryl requires neutralization and heating to be incorporated into 10 standard creams. In one embodiment, the present invention utilizes a new manufacturing method, whereby dissolving the Dermacryl in the ethanol first, then combining this with the warm oil phase (40-45°C) before forming the emulsion has the advantage of not having to heat the ethanol, thus providing a safer 15 method of manufacture than traditional techniques where a hot oil/ethanol phase is added to a hot water phase.

The acrylic copolymer with carboxyl groups such as Dermacryl 79, is insoluble in water, thereby imparting wash resistance in a formulation. If the carboxyl groups are fully neutralized, the acrylic copolymer would be water soluble, hence impart no wash resistance. A partially neutralized copolymer (for 20 example, 29% neutralization), has been surprising found to show enhanced water solubility over an un-neutralised formulation, and improved wash resistance over a fully neutralized formulation. An example of a fully (100%) neutralized formula is given below: An example of a fully (100%) neutralized formula is given below in Table 1:

25

Table 1

Item No.	Ingredient	%w/w
1	Purified Water	52.11
2	Sodium Benzoate	0.19
3	EDTA di-Sodium	0.10
4	Polawax GP200	2.85
5	Parsol MCX	7.13
6	Uvinul M40	3.80
7	Parsol 1789	1.90
8	Crillet 45	0.83

Item No.	Ingredient	%w/w
9	Ethomeen C25	3.92
10	Dermacryl-79	1.90
11	Ethanol SDA 40-2	20.27
	TOTAL	95.00

plus propellant at 5%w/w.

The effect of partially neutralized and fully neutralized Dermacryl-79 in the formulation was investigated. SPF results of the formulations are shown below:
100% neutralized Dermacryl 79 - SPF 3.9 (40-minutes wash resistance) Table 1.

- 5 29% neutralized Dermacryl 79 - SPF 16.1 (40-minutes wash resistance) (Table 3).

d) **Neutralization of Dermacryl**

- Dermacryl 79 is carboxylated and is normally neutralized with a suitable alkaline material in formulation. The formulator can use materials such as 10 triethanolamine, 2-amino-2-methyl-1-propanol, ammonium or potassium hydroxides, or long chain amines. The amount of base required to neutralize the carboxyl groups in DERMACRYL 79 can be determined by the following relationship: $B = \frac{Wx2.4xNxE}{1000}$

- Where: B = weight (grams) of base needed; W = weight (grams) of 15 DERMACRYL 79 used; N = % neutralization required (decimal); and E = equivalent weight of base (eq/g). A specific example of 100% neutralization of 100 grams of DERMACRYL 79 with triethanolamine is as follows: EXAMPLE: W = 100 grams; N = 1.00; E = 149.2; B = $\frac{100x2.4x1.00x149.2}{1000} = 35.8$ grams TEA.

- Tables 2 and 3 show different SPF 15 foam compositions of the present 20 invention. The partially neutralized formula is set forth below (Table 3).

Table 2: SPF 15 Foam

Trade Name	% w/w (No propellant)	% w/w (with propellant)
Ethanol SDA 40-2	24.96	23.71
Dermacryl 79	2.00	1.90
Polawax GP200	3.00	2.85
Parsol MCX	7.50	7.13
Uvinul M40	4.00	3.80

Trade Name	% w/w (No propellant)	% w/w (with propellant)
Parsol 1789	2.00	1.90
Myrj 52	1.20	1.14
Purified Water	54.24	51.53
Sodium Benzoate	0.20	0.19
di-sodium EDTA	0.10	0.095
Crillet 1	0.80	0.76
Propellant P70	0	5.00

Table 3: SPF 15 Foam

Trade Name	% w/w (No propellant)	% w/w (with propellant)	Function
Deionized Water	56.30	53.49	Solvent
Alcohol SDA 40-2	21.90	20.81	Solvent
Parsol MCX	7.50	7.13	Sunscreen-UVB
Propellant P45	0.00	5.00	Propellant
Uvinul M-40	4.00	3.80	Sunscreen-UVA
Polawax GP200	3.00	2.85	Emulsifier
Myrj 52	2.13	2.02	Emollient
Parsol 1789	2.00	1.90	Sunscreen-UVA
Dermacryl-79	2.00	1.90	Film Former
Crillet 45	0.87	0.83	Emulsifier
Sodium Benzoate	0.20	0.19	Anti-corrosion protection
di-sodium EDTA	0.10	0.10	Chelating agent

2. Example 2

This example illustrates a method of manufacturing the compositions of the present invention.

5 The sunscreen formulations of the present invention can be produced using the following procedure. The particle size and emulsion appearance were assessed using an Olympus BX50 microscope. The ambient manufacturing method of manufacture is set out below:

a) Water Phase:

- 10 1. Weigh purified water into a vessel. Heat to 45-50°C.
 2. While stirring add Myrj 52, continue to stir until the Myrj 52 has dissolved.
 3. While stirring, add Sodium Benzoate, stir until dissolved.
 4. While continuing to stir the product, add Disodium EDTA, stir until dissolved.

5. Stir cool to 20-30°C.

6. Correct for any loss of water.

b) Ethanol Phase:

7. Weigh Ethanol into a separate tank.

5 8. While stirring, slowly add Dermacryl 79, continue to stir until dissolved.

Oil Phase:

9. Weigh Parsol MCX into a separate vessel and heat to 50 - 55°C.

10. While stirring, add Crillet 45, Uvinul M40, Parsol 1789 and Polawax GP200, continue to stir until all components have dissolved.

10 11. Stir cool to 40-45°C.

12. While stirring, slowly add the oil phase to the ethanol phase and continue to stir until dissolved.

13. Correct for any loss of Ethanol.

14. Maintain at 20-30°C.

15 **c) Emulsion Formation:**

15. While stirring the water phase, slowly add the Ethanol/Oil phase into the vortex.

16. Homogenise batch until the particle size is within specification.

17. Slow stir to allow the batch to de-aerate.

20 **3. Example 3**

This example shows percent neutralization can have an effect on water resistance.

As shown below in Table 4, 0% and 25% neutralization show exceptional water resistance capabilities.

25 The in vitro water resistance testing involves applying an accurately weighed mass of sunscreen foam formulation to an accurately weighed substrate (ie glass microscope slide). The product is placed in an incubator and allowed to dry to a film.

The substrate with the dried film is placed into a waterbath with shaking , after which it is returned to an incubator and redried.

The water resistance of each film is calculated as the percentage of film remaining on the substrate.

- 5 The results indicate that at 0% neutralization and at 25% neutralization of the Dermacryl, the water resistance of the film was higher than the 100% neutralized film. While the partial neutralization of the Dermacryl allowed it to be solubilised in the formulation, the formulation still provided good water resistance.
- 10 From this, it can further be expected that the partially neutralized Dermacryl formulation would provide better SPF than the 100% neutralized Dermacryl formulation post immersion in water.

Table 4

Product:	Sunscreen Foam F210/04/05 E210/04/05 30% EtOH 25% Neutralization		Sunscreen Foam F210/04/13 E210/04/13 10% Ethanol 0% Neutralization		Sunscreen Foam F210/04/18 E210/04/18 10% Ethanol 100% Neutralization	
	1	2	1	2	1	2
Wt of microscope slide (T):	16.8371	17.2195	16.7635	16.7936	17.5840	17.1021
Wt of microscope slide plus product:	18.1036	18.3680	17.7508	17.8898	18.6974	18.1176
*Wt of product applied to microscope slide:	1.2665	1.1485	0.9873	1.0962	1.1134	1.0155
After 15hrs at 25°C/ 5mins at ambient	17.0993	17.4681	16.9861	17.0297	17.8473	17.3413
After 60mins at 50°C/5mins at ambient	17.0953	17.4641	16.9861	17.0264	17.8445	17.3392
After 135mins at 50°C/ 5mins at ambient	17.0939	-	-	17.0258	17.8442	17.3390
After 180mins at 50°C/ 5mins at ambient	-	17.4628	16.9860	-	-	-
After 210mins at 50°C/ 5mins at ambient	-	-	-	-	-	-
$\langle MF1 \rangle$	17.0939	17.4628	16.9860	17.0258	17.8442	17.3390

Immerse in static waterbath at 25°C for 20 mins

60mins at 50°C/ 5 mins at ambient	-	17.4000				
90mins at 50°C/ 5 mins at ambient	17.0281					
140mins at 50°C/ 5 mins at ambient	17.0169					
170 mins at 50°C/ 5 mins at ambient	17.0119					
After 62hrs at 25°C/ 5 mins at ambient	16.9976					
120 mins at 50°C/ 5 mins at ambient	16.9964					
$\langle MF2 \rangle$	16.9964	17.3833	16.9201	16.9461	17.6531	17.1623

Washability (in water) - % Weight Loss	62	67	70	66	27	25
AVERAGE WATER RESISTANCE	65		68		26	

The foregoing discussion of the invention has been presented for purposes of illustration and description. The foregoing is not intended to limit the invention to the form or forms disclosed herein. Although the description of the invention 5 has included description of one or more embodiments and certain variations and modifications, other variations and modifications are within the scope of the invention, e.g., as may be within the skill and knowledge of those in the art, after understanding the present disclosure. It is intended to obtain rights which include alternative embodiments to the extent permitted, · including alternate, 10 interchangeable and/or equivalent structures, functions, ranges or steps to those claimed, whether or not such alternate, interchangeable and/or equivalent structures, functions, ranges or steps are disclosed herein, and without intending to publicly dedicate any patentable subject matter.

CLAIMS:

1. A composition in a pressurized container for forming a hydroalcoholic foam, said composition comprising:
 - 5 at least one active agent;
 - a water insoluble film-forming polymer;
 - a hydroalcoholic foaming agent; and
 - an aerosol propellant.
2. The composition of Claim 1, wherein said active agent comprises a sunscreen component.
- 10 3. The composition of Claim 2, wherein said sunscreen component comprises at least one UVB sunscreen and/or at least one UVA sunscreen.
4. The composition of Claim 2, wherein said sunscreen component is selected from the group consisting of octinoxate, oxybenzone, butyl methoxydibenzoylmethane, and a mixture thereof.
- 15 5. The composition of Claim 1, wherein said water insoluble film-forming polymer forms a water resistant film.
6. The composition of Claim 1, wherein said film-forming polymer is a water insoluble carboxylated acrylic copolymer selected from the group consisting of acrylate/t-octylpropenamide, octylacrylamide/acrylate/butylaminoethyl methacrylate copolymer, acrylates/octylacrylamide copolymer, and a mixture thereof.
- 20 7. The composition of Claim 6, wherein said water insoluble carboxylated acrylic copolymer is acrylates/octylacrylamide copolymer.
8. The composition of Claim 7, wherein a percentage of the carboxylic acid groups that is present in said water insoluble carboxylated acrylic copolymer is neutralized.

9. The composition of Claim 8, wherein said percentage neutralized is between about 0% to about 40 %.
10. The composition of Claim 8, wherein said percentage neutralized is between about 3% to about 35 %.
- 5 11. The composition of Claim 8, wherein said percentage neutralized is between about 7% to about 33%
12. The composition of Claim 8, wherein said carboxylated acrylic copolymer is neutralized using sodium benzoate.
13. The composition of Claim 1, wherein the amount of alcohol is about 40%
10 or less by weight of the total composition.
14. The composition of Claim 1, wherein the amount of alcohol is about 25% or less by weight of the total composition.
15. The composition of Claim 3, further comprising a chelating agent.
16. The composition of Claim 15, wherein said chelating agent is tetrasodium
15 EDTA.
17. The composition of Claim 6, further comprising a surfactant.
18. The composition of Claim 17, wherein said surfactant comprises polyoxyalkylene stearyl ester, cetearyl alcohol, polysorbate or mixtures thereof.
19. The composition of Claim 18, wherein said polyoxyalkylene stearyl ester is
20 polyethylene glycol stearyl ester.
20. The composition of Claim 18, wherein said surfactant comprises a mixture of PEG-40 stearate, PEG-20 stearate, cetearyl alcohol and polysorbate 85.

21. The composition of Claim 1, wherein the melting point of said hydroalcoholic foam is about 40°C or higher.
22. The composition of Claim 21, wherein said composition in said pressurized container is an emulsion.
- 5 23. The composition of Claim 21, wherein said hydroalcoholic foaming agent comprises a C₁-C₆ alcohol, water, wax and a surfactant.
24. The composition of Claim 21, wherein said composition forms a foam when released from the container.
- 10 25. A sunscreen composition in a pressurized container comprising:
 - a sunscreen component comprising at least one UVB sunscreen and/or at least one UVA sunscreen;
 - a hydroalcoholic foaming agent; and
 - an aerosol propellant.
26. The composition of Claim 25, further comprising a water insoluble film-forming polymer.
- 15 27. The composition of Claim 26, wherein said film-forming polymer is a water insoluble carboxylated acrylic copolymer selected from the group consisting of acrylate/t-octylpropenamide, octylacrylamide/acrylate/butylaminoethyl methacrylate copolymer, acrylates/octylacrylamide copolymer, and a mixture thereof.
- 20 28. The composition of Claim 27, wherein the total amount of said water insoluble film-forming polymer is from about 0.1% to about 10% by weight of the total composition.
29. The composition of Claim 26, wherein said sunscreen component is selected from the group consisting of: Aminobenzoic acid (4-Aminobenzoic acid); Avobenzene (4-tert-butyl-4-methoxydibenzoylmethane); Benzophenone-2

- (Bis(2,4-Dihydroxyphenyl) Methanone); Benzophenone-3 (Oxybenzone); Benzophenone-4 (Sulisobenzene); Benzophenone-5 (Sulisobenzene sodium); Benzophenone-8 (Dioxybenzone); Benzylidene Camphor (3-(4-Methylbenzylidene)-d-1camphor); Cinoxate; Ecamsule (Terephthalylidene dicamphor sulfonic acid); Ethoxylated ethyl 4-aminobenzoic acid (PEG25 PABA); Homosalate (Homomethyl salicylate); Isoamylmethoxycinnamate (Isopentenyl-4-methoxycinnamate); Isopropylbenzyl salicylate; Menthyl anthranilate (Methyl 2-aminobenzoate); Mexoryl XL (phenol,2-(2H-benzotriazol-2-yl)-4-methyl-6[2-methyl-3-[1,3,3,3-tetramethyl-1-[(trimethylsilyl)oxy]disiloxanyl]propyl) Octyl dimethyl PABA; Octinoxate (Octyl methoxycinnamate); Octyl salicylate (2-Ethylhexyl Salicylate); Octocrylene (2-cyano-3,3-diphenyl acrylic acid,2-ethyl hexyl ester); Octyl triazole (2,4,6-Trianalino-(p-Carbo-2'-ethylhexyl-1'oxy)1,3,5-Triazine); Padimate O (2-Ethylhexyl 4-dimethylaminobenzoate); Phenylbenzimidazole sulfonic acid (2-Phenylbenzimidazole-5-sulfonic acid) and its potassium, sodium and triethanolamine salts; N,N,N-Trimethyl-4-(oxoborn-3-ylidenemethyl) anilinium methylsulfate; Salicylic acid salts (potassium,sodium and triethanolamine); Tinosorb M (2,2'-Methylene-bis-6-(2H-benzotriazol-2yl)-4-(tetramethyl-butyl)-1,1,3,3-phenol); Titanium dioxide; Triethanolamine salicylate; Zinc oxide; and a mixture thereof.
- 20 30. The composition of Claim 29, wherein said sunscreen component comprises octinoxate, oxybenzone, butyl methoxydibenzoylmethane or a mixture thereof.
- 25 31. The composition of Claim 29, wherein said sunscreen component comprises a mixture of octinoxate, oxybenzone and butyl methoxydibenzoylmethane.
32. The composition of Claim 29, wherein the total amount of said sunscreen component is from about 5% to about 30% by weight of the total composition.
33. A sunscreen composition in a pressurized container comprising water; a C₁-C₆ alcohol; a wax; a sunscreen component comprising at least one UVB

sunscreen and at least one UVA sunscreen; a surfactant; a propellant; and a water insoluble film-forming polymer, wherein said composition is a hydroalcoholic foam after release from the container.

34. The sunscreen composition of Claim 33, wherein the amount of C₁-C₆ alcohol is about 40% or less by weight of the total composition.

35. The sunscreen composition of Claim 33, further comprising a chelating agent.

36. The sunscreen composition of Claim 35, further comprising an anti-corrosion protection agent.

10 37. A method for protecting human skin from the harmful effects of ultraviolet light comprising topically applying to the skin an effective amount of a hydroalcoholic foam as claimed in Claim 1 or a sunscreen composition as claimed in Claim 25..

15 38. The method of Claim 37, wherein the hydroalcoholic sunscreen foam forms a water resistant film of sunscreen on the applied skin.

39. The method of Claim 38, wherein the hydroalcoholic sunscreen foam comprises a sunscreen component and a water insoluble film-forming polymer that is capable of forming a water resistant film of sunscreen on the applied skin.

20 40. The method of Claim 39, wherein the film-forming polymer is a water insoluble carboxylated acrylic copolymer selected from the group consisting of acrylate/t-octylpropenamide, octylacrylamide/acrylate/butylaminoethyl methacrylate copolymer, acrylates/octylacrylamide copolymer, and a mixture thereof.

25 41. The method of Claim 40, wherein the sunscreen component comprises octinoxate, oxybenzone, butyl methoxydibenzoylmethane or mixtures thereof.

42. Use of a hydroalcoholic foam as claimed in Claim 1 or a sunscreen composition as claimed in Claim 25 for the protection of human skin from the harmful effects of ultraviolet light.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2004/000170

A. CLASSIFICATION OF SUBJECT MATTER		
Int. Cl. ⁷ : A61K 7/44, A61K 7/42, A61K 7/40, A61P 17/16		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) DWPI, CAS. Keywords: sunscreen(s) and foam(s).		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BATTISTINI, G., Rivista Italiana Essenze, Profumi, Piante Officinali, Aromi, Saponi, Cosmetici, Aerosol, 1966, vol 98(7), 422-7 Abstract	25, 37, 38, 42
A	WO 2003/011238 A (MERCK PATENT GMBH), 13 February 2003 Whole document	1-42
A	WO 2001/005366 A (PLAYTEX PRODUCTS, INC), 25 January 2001 Whole document	1-42
<input type="checkbox"/> Further documents are listed in the continuation of Box C		<input checked="" type="checkbox"/> See patent family annex
<p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p>		
Date of the actual completion of the international search 16 March 2004	Date of mailing of the international search report - 7 APR 2004	
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer G.J. MCNEICE Telephone No : (02) 6283 2055	

Best Available Copy

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU2004/000170

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Member		
A WO2003/011238			
A WO 2001/005366	AU 200061065	EP 1 200 054	END OF ANNEX

Best Available Copy